

Long-term results of liver transplantation from donation after circulatory death

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Abbreviations in alphabetical order

1st WIT, first warm ischemia time (time from stop circulation till aortic cold perfusion)

ARDS, acute respiratory distress syndrome

CIT, cold ischemia time

DBD, donation after brain death

DCD, donation after circulatory death

DRI, donor risk index

ELIAC, Eurotransplant Liver Intestine Advisory Committee

ET, Eurotransplant

ET-DRI, Eurotransplant donor risk index

GGT, gamma glutamyl transpeptidase

HR, hazard ratio

LT, liver transplantation

ITBL, ischemic-type biliary lesions (or NAS, non-anastomotic strictures)

MELD, model for end-stage liver disease

MOF, multi organ failure

NAS, non-anastomotic strictures

PNF, primary non-function

SD, standard deviation

SRTR, Scientific Registry of Transplant Recipients

UNOS, United Network for Organ Sharing;

Abstract

Donation after circulatory death (DCD) liver transplantation (LT) may imply a risk for decreased graft survival, caused by post-transplantation complications such as primary non-function or ischemic-type biliary lesions. However, similar survival for DCD and donation after brain death (DBD) LT has been reported. Objective of this study is to determine long-term outcome of DCD LT in the Eurotransplant region corrected for Eurotransplant donor risk index (ET-DRI). Transplants performed in Belgium and The Netherlands (1.1.2003 - 31.12.2007) in adult recipients were included. Graft failure was defined as either date of recipient death or retransplantation; death un-censored graft survival. Mean follow-up was 7.2 years. In total 126 DCD and 1264 DBD LT's were performed. Kaplan-Meier survival analyses showed different graft survival for respectively DBD and DCD at one (78% vs. 75%, $p=0.71$), five (66% vs. 54%, $p=0.02$) and ten (47% vs. 44%, $p=0.55$) years (Log Rank $p=0.038$). Although there was an overall significant difference, the survival curves almost reach each other after 10 years, most probably caused by lower other risk factors in DCD livers. Patient survival was not significantly different ($p=0.59$). Multivariate Cox-regression analysis showed a HR 1.7 ($p<0.001$) for DCD (corrected for ET-DRI and recipient factors). First warm ischemia time (1st WIT) over 25 minutes was associated with a lower graft survival in univariate analysis of all DCD transplants ($p=0.002$). **Conclusions:** DCD LT has an increased risk for diminished graft survival compared to DBD. There was no significant difference in patient survival. DCD allografts with a 1st WIT>25 minutes give an increased risk for decreased graft survival.

Introduction

Donation after circulatory death (DCD) is known to be one of the most important donor risk factors for worse outcome after liver transplantation (LT). Previous studies have reported a hazard ratio (HR) of 1.51 in the United Network for Organ Sharing (UNOS) (1) and 1.71 in Eurotransplant (ET) (2). Post-transplant complications such as ischemic-type biliary lesions (ITBL) and primary non-function (PNF) occur more often, resulting in higher retransplantation rates. (3-6) Still, similar results for grafts from controlled DCD donors compared with grafts from donation after brain death (DBD) donors have been reported from the initial series from The Netherlands, with a higher retransplantation rate in the DCD-group due to biliary problems, (7) whereas a large study with data from the Scientific Registry of Transplant Recipients (SRTR), investigating DCD and DBD outcome, found decreased survival for the DCD group. (8) This indicates that the use of controlled DCD donors could be a justified alternative source for livers next to DBD donors, when bearing this additional risk in mind. Some studies even reported equally good early outcome for extended criteria DCD grafts as compared to standard DCD grafts. (9) The same conclusions came from several (recent) reports from Belgium (10-12) and The Netherlands (7,13).

Studies investigating risk factors in DCD liver transplantation found certain donor factors, such as age, weight, cold and warm ischemia time to be significantly associated with graft failure after DCD liver transplantation. (14,15) Since the DCD procedure itself leads to a certain first warm ischemia time (1st WIT), which is potentially harmful to the liver, only donors with little other risk factors are being evaluated and stricter criteria for donation are used compared to DBD donors. Furthermore, patients can be selected by MELD score as recipient in order to acquire the optimal result or highest benefit. (16-18) Unfortunately, there are few studies investigating the long-term effect of DCD on outcome after LT.

The objective of this study is to investigate the long-term outcome for DCD liver transplantation within the ET region and evaluate the effect of DCD versus DBD, adjusted for the ET donor risk index (ET-DRI) and recipient risk factors.

Patients and Methods

This study is a retrospective analysis of all deceased donor liver transplants performed in Belgium and The Netherlands into adult (≥ 18 years) recipients during the period from January 1st 2003 till December 31st 2007. Transplants performed in countries that did not perform DCD transplants (Austria, Croatia, Germany, Luxemburg and Slovenia) in this dataset (N=4549) and transplants performed with liver allografts from outside Eurotransplant (N=89) were excluded. Follow-up data of all 1390 liver transplants were obtained from the Eurotransplant database in March 2015, with consent of the Eurotransplant Liver Intestine Advisory Committee (ELIAC). All data were anonymized for transplant center and country.

Data selection

In the study period DCD liver transplants were only performed in two Eurotransplant countries (Belgium and The Netherlands) and therefore only the transplants performed in these countries were used in the analysis (N=1390). There were 98 missing values (7.1%) in the follow-up data (patients lost to follow-up). The remaining 1292 transplants were used in the survival analysis. The DRI (1) and ET-DRI (2) were calculated for all donors when all factors were available. As race is not registered in the Eurotransplant database, all donors were regarded as reference (Caucasian) when calculating the DRI. Since 'national sharing' within UNOS is different than 'national sharing' within Eurotransplant, all countries, except for Germany, were regarded as one donor region within Eurotransplant. National sharing was considered as extra-regional sharing, meaning sharing within the whole of Eurotransplant. Due to missing cold ischemia times (CIT) or most recent gamma glutamyl transpeptidase (GGT), it was not possible to calculate the DRI for 275 donors and the ET-DRI for 290 donors; these transplants were therefore not included in the analysis with DRI/ET-DRI.

Statistical analysis

Graft survival (death un-censored) was defined as the period from date of transplantation until date of retransplantation or recipient death, whichever occurred first. There is no 'general agreement' within the ET region or between the ET member states on strategies for retransplantation, leading to a different situation for each individual transplant center. Some centers may treat biliary complications with interventions whereas other centers may choose for a retransplantation faster.

First warm ischemia time was defined as time from stop circulation till start of cold organ perfusion. For the analysis of first warm ischemia time, five subgroups were created: <10 minutes, 10-15 minutes, 16-20 minutes, 21-25 minutes and >25 minutes. Clinical characteristics were summarized in mean and standard deviation (SD) for continuous variables or number and percentage for categorical factors. Comparison between groups was done using Chi-square (categorical factors) or Student's t-test (continuous factors). Survival analyses were performed using Kaplan-Meier survival curves and multivariate analyses were performed using Cox regression models. For all analyses a Wald p-value of $p < 0.05$ was considered significant. Statistical analyses were performed with SPSS, version 23.0.

Results

In total 126 DCD and 1264 DBD liver transplants were performed in the study period, with a mean follow-up of 7.2 years. Donor and transplant characteristics of the two groups are displayed in Table 1. Significant differences between DCD and DBD were lower donor age (41 years vs. 47 years, $p < 0.001$), less cerebrovascular accidents in the DCD-group 41% vs. 59% ($p < 0.001$), no split liver in the DCD-group ($p = 0.02$), mostly local and regional allocation ($p < 0.001$) and lower CIT in the DCD-group (7.2h vs. 8.9h, $p < 0.001$). There was a higher percentage of rescue allocation in the DCD-group (26% vs. 12%, $p < 0.001$), which was the only other factor with increased risk in the DCD-group.

Mean DRI and ET-DRI of DCD donors were higher as compared to the DBD-group, respectively DRI 2.0 vs. 1.6 ($p < 0.001$) and ET-DRI 2.1 versus 1.7 ($p < 0.001$). When the factor DCD was excluded from the (ET-) DRI calculation, the mean values in the DCD-group were much lower compared to the DBD-group: DRI 1.3 vs. 1.6 ($p < 0.001$) and ET-DRI 1.4 vs. 1.7 ($p < 0.001$).

Recipient factors are displayed in Table 1. Recipients transplanted with a DCD liver allograft were slightly older, however not significantly ($p = 0.42$), more often male ($p = 0.02$), had a significant lower mean MELD score (16 vs. 20, $p < 0.001$) and a lower percentage of high urgent transplantation (5% vs. 15%, $p = 0.002$). DCD allografts were transplanted significantly less often in retransplantation candidates (5% vs. 15%, $p = 0.002$).

Long-term outcome of DCD vs. DBD

Kaplan-Meier survival curves showed different graft survival rates for DCD versus DBD (Log Rank $p=0.038$) (Figure 1 and Table 2), meaning there were more added life-years / grafts last longer after transplantation of a DBD liver compared to a DCD liver (reflected in area under the curve). Specific graft survival at one (75% vs. 78%, $p=0.71$), five (54% vs. 66%, $p=0.02$) and ten years (44% vs. 47%, $p=0.55$) showed that the differences in graft survival increased in the first 5 years and decreased in the following years, leveling out at around 10 years post-transplantation.

Univariate Cox regression analysis gave a hazard ratio (HR) of 1.31 (95% CI 1.01-1.69, $p=0.04$) for DCD compared to DBD. There was no significant difference in patient survival between DCD and DBD at the previously named time points ($p=0.59$; Table 2). Interestingly, patient death was not significantly different, but there was a significantly higher chance for retransplantation after DCD LT. Reasons for patient death or retransplantation are shown in Table 3. Thrombosis was a relatively more frequent cause of retransplantation after DBD LT (1.7% vs. 0.8%), whereas the DCD recipients had a higher percentage of PNF, 3.2% vs. 0.7%, and non-anastomotic strictures (NAS) 6.3% vs. 0.6% ($p=0.002$).

Multivariate analysis

Multivariate Cox regression analyses of the 'DCD factor' in relation to graft survival, corrected for other factors in the DRI, ET-DRI and all available recipient factors (age, MELD, high urgent status, cause of end-stage liver disease, retransplantation status), gave a HR of respectively 1.86 (95% CI 1.38-2.52, $p<0.001$) (for DRI factors) and 1.81 (95% CI 1.33-2.47, $p<0.001$) (for ET-DRI factors).

When the DCD was corrected for the calculated DRI and ET-DRI, (calculated without the factor DCD) and recipient factors, it remained significantly associated with graft survival with a HR of respectively 1.73 (95% CI 1.30-2.30, $p<0.001$) (DRI) and 1.70 (95% CI 1.27-2.25, $p<0.001$) (ET-DRI). This also confirms the strong correlation between the DRI, ET-DRI and DCD.

Sub analysis of first warm ischemia time

Next, a sub-analysis of the DCD-group was performed ($N=126$) to investigate the influence of the 1st WIT. Mean 1st WIT was 14 (range 4-38) minutes. Kaplan-Meier survival analysis of the 1st WIT divided into five categories (see Methods) not significantly associated with graft survival (log rank

test $p=0.12$), but showed the impact of 1st WIT>25 minutes (Table 4). When performing an univariate analysis with the cut-off at 25 minutes, there was a significant correlation with graft survival (HR3.11, 95% CI 1.24-7.79, $p=0.02$). Multivariate Cox regression analysis of this factor, corrected for the ET-DRI, showed a trend towards a significant correlation with graft survival when divided into five categories ($p=0.11$) and when using a cutoff of 25 minutes it was significant (HR3.53, 95% CI 1.38-9.04, $p=0.009$). Figure 2 shows the Kaplan Meier survival curve for patients that were transplanted with a liver allograft that sustained >25 minutes of WIT compared with grafts with a WIT≤25 minutes.

Discussion

This study investigated the risk of DCD liver transplantation within two countries belonging to the ET region, Belgium and The Netherlands, with long-term follow-up and aimed to adjust the increased risk of the 'factor DCD' by using the DRI and ET-DRI.

The results show that it seems that by adequate selection of DCD allografts the additional risk of a DCD procedure can be kept to a minimum. This is actually clinical practice, because when excluding DCD as a factor from the DRI and ET-DRI, the risk indices became much lower for the DCD-group (DRI 1.3 and ET-DRI 1.4) as compared to the mean (ET-)DRI of the DBD group. This indicates that DCD donors indeed have better 'other' donor characteristics, such as lower donor age, less CVA as cause of death, lower cold ischemia time and no split liver donation.

The recipient characteristics between the DBD and DCD group differed in relation to recipient MELD score, percentage of HU-status and repeated transplantation; DCD recipients were in better condition. The results also show that there seems to have been an increased frequency of infections in the DCD group (6.3% vs. 3.8% in the DBD group). We tried to look for a possible relation with the occurrence of biliary complications, however it was impossible to distract any clear correlation from the provided data of the 11 centers.

In the Kaplan-Meier curve graft survival at five years was worse in the DCD group (Figure 1), but this difference leveled out after ten years follow-up. Patient survival rates were not significantly different in DCD and DBD grafts at any time in follow-up (Table 2). This means that there is a higher chance for graft failure and subsequent retransplantation within the first five years after DCD LT, probably explained by the higher incidence of biliary complications (ITBL/NAS) in DCD grafts. (15,19) After

five years the failure risk for DCD allografts is lower when compared to DBD allografts, which might be explained in turn by the younger donor age and better condition of recipients at the time of LT. As transplant physicians take patients disease and current situation into account when accepting organs, they might decide to accept or decline a DCD liver allograft, knowing the potential risks of this allograft after LT. Also the consent of the patient is something that could play a role in the acceptance of such a liver allograft.

When correcting for recipient factors and ET-DRI in the multivariate analysis the factor DCD is a very significant risk factor with a high hazard ratio (HR 1.7, $p < 0.001$). This study is the first to show this additional risk by correcting for other factors that could influence outcome (donor, transplant and recipient factors) by using the ET-DRI. A recent study by Singhal *et al.* found similar results in a matched controlled analysis with data of the SRTR database: DCD donors were younger, had shorter CIT's and recipients had lower MELD scores. Another finding in that study was the significantly higher associated costs and a higher re-admission rate for DCD recipients, (20) comparable to data from the Netherlands. (21) The difference in graft survival as compared to the earlier study by Dubbeld *et al.* (7) might be due to the acceptance of increasing risk factors when getting more acquainted with the DCD procedure over time and a larger sample size.

This study has several limitations such as the retrospective study design and the recipient selection bias, as this selection was already done by the recipient center. However, we minimized this effect by correcting for donor and recipient factors. Another limitation is the selected endpoint of combined patient and graft survival (death un-censored graft survival) as only outcome parameter. In order to do a good interpretation of the problems after DCD liver transplantation biliary complications such as ITBL (or NAS) should also be taken into account as an end-point. Unfortunately these data are not standard registered in the ET database. Nevertheless, cases of severe biliary damage will eventually lead to retransplantation, which was taken as an endpoint in this study. Another limitation was the fact that in 275 cases the DRI and in 290 the ET-DRI could not be calculated due to missing CIT or GGT in the ET database. Lastly, the survival curves almost reach each other at ten years, but the percentage of patients in the analysis at ten years follow-up was lower than ten percent of the total number of patients in that subgroup.

The factor 1st WIT was demonstrated to have an important impact on outcome in DCD LT. Donor WIT above the cut-off value of 25 minutes significantly correlated with worse outcome ($p=0.011$).

When analyzing this factor more in detail by creating five different WIT groups there was no significant correlation with graft survival, but there was a clearly lower graft survival if the 1st WIT encompassed 25 minutes (graft survival of 17%). Although the risk of increased 1st WIT has already been described in previous studies in relation to the higher chance for primary non-function, graft dysfunction or biliary strictures (10,22), this study shows this risk after LT when correcting for the ET-DRI in the multivariate analysis. Accepting of a liver graft with 1st WIT above 25 min, should probably only be considered for specific cases, and only if other risk factors are kept low (donor age, CIT, etc.). Another option could be to look for strategies to decrease the risk of the 1st WIT to exceed 25 minutes, for example by withdrawal of ventilatory support in the operating room as is standard protocol in Belgium. Within The Netherlands the standard procedure is to perform the withdrawal of ventilatory support in the intensive care unit (ICU). After the death is declared at the cessation of circulation, there is a mandatory no-touch period of 5 minutes, in which period the donor may be transported to the OR. In Belgium this period varies from 2 till 4 minutes (10,23), leading to a minimal 1st WIT of 2-5 minutes. Practical issues such as transport of the donor from ICU to the operating room and preparation for the organ perfusion might lead to additional 1st WIT, especially in The Netherlands. Obviously there are selected cases in which the perfusion exceeds the preferred time limit of 25 minutes, but as our results show, this only occurs incidentally. Technical issues (or lack of) do not seem to be related to these sometimes 'longer' 1st WIT periods since all involved surgeons in The Netherlands and Belgium are specifically trained in and certified for multi-organ donation procedures.

In the ET region the definition of the 1st WIT is defined as: *'time from cardiac arrest until perfusion of the donor'* (ET manual, Ch. 9). This is a clear agreement made by the ET countries. The problem is however that different definitions are used worldwide and that the more common definition is the time period from withdrawal of ventilation till start of cold organ perfusion. This issue has been already addressed previously. (10,23) Nevertheless, a clear and unambiguous definition remains important and should be looked at more carefully, as was for example done by Taner *et al.* in a recent UK study. (24,25) Unfortunately clinical donor data with regard to the withdrawal of life

support procedure (e.g. oxygen saturation or mean arterial pressure values) were not recorded in this ET dataset and could unfortunately not be investigated.

Within the Netherlands there is a strict protocol for selecting DCD donors: 'the Dutch protocol for organ donation'. This protocol upholds certain criteria for DCD liver allograft donation in The Netherlands, such as maximum donor age of 60 years. (26) In 2013 the percentage of DCD liver transplantation was 22% in Belgium and even as high as 38% in the Netherlands. (27) Although the DCD procedure holds certain risks, such as increased rates of biliary complications, hepatic artery stenosis or decreased outcome, it provides a valuable source for donor liver allografts in this time of organ scarcity. Univariate graft survival between the two groups was comparable, but significantly better in the DBD group. When looking at other risk factors such as donor age and CIT for DCD donors, almost equally good results can be achieved. This was advised in the recent British Transplantation Society guidelines for DCD transplantation. (28) Nevertheless, the possibly poorer quality of life of patients with biliary strictures should also be taken into account.

The risk of DCD LT is well known, so several measures to improve results are proposed such as the limitation of the 1st WIT and CIT (which are modifiable risk factors). There is also a need to implement innovative strategies to ameliorate graft quality, such as donor preconditioning using in situ reconditioning (with the use of extracorporeal machine oxygenation (ECMO)) or post procurement reconditioning by use of machine perfusion. (29) At the time of the organ offer, the 1st WIT is mostly not known since the DCD procedure is yet to start. After the organ recovery the 1st WIT is known and one of the factors that could be influenced to mitigate for a longer 1st WIT is the CIT. Solutions for shortening this CIT is by local or national allocation, which is currently the case in Belgium and The Netherlands. Another factor that could correct for a potentially longer 1st WIT is lower donor age. As shown in this study, the ET-DRI (without the factor DCD) is significantly lower in DCD donors, with age being a major factor in the ET-DRI calculation and also being significantly lower as compared to DBD donors. Nevertheless, recent studies did not find any difference in outcome for younger or older DCD donors and concluded that a DCD donor should not be discarded purely based on age, since increased donor age did not contribute to graft failure after DCD liver transplantation. (12,30)

In conclusion, this is the first European study to evaluate long-term outcome of LT using circulatory death donors. DCD is confirmed to be a risk factor causing a significantly decreased graft survival after LT in Belgium and The Netherlands (HR 1.7, $p < 0.001$). This difference in graft survival peaks at five years, but seems to flatten out afterwards. Patient survival did not significantly differ and this should therefore encourage the use of DCD liver allografts.

Altogether, recipients of a DCD liver have a higher risk of graft loss within the first five years after transplantation (due to biliary complications such as ITBL), but if this is not the case, the graft survival tends to be better than with a DBD liver graft, probably due to the lower donor age and on average the better condition of the recipient at time of transplantation. First warm ischemia time longer than 25 minutes has a significant risk for decreased outcome after DCD liver transplantation and when exceeding 25 minutes the majority of transplanted DCD livers failed.

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Figure legends

Figure 1:

Long-term graft survival for DCD and DBD transplantations (log rank test $p=0.038$)

- Green line: DCD transplantations
- Blue line: DBD transplantations

Figure 2:

Long-term graft survival for first warm ischemia time categories (log rank test $p=0.011$)

- Green line: 1st WIT >25 minutes
- Blue line: 1st WIT ≤ 25 minutes

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Table 1: donor, transplant and recipient characteristics for DBD (N=1264) and DCD (N=126)

Factor	DBD	DCD	p-value
	N (%)	N (%)	
Female donor	597 (47)	49 (39)	0.07
Cause of death			<0.001
CVA	749 (59)	51 (41)	
Trauma	406 (32)	38 (30)	
Anoxia	61 (5)	22 (18)	
Other	48 (4)	15 (12)	
Split liver	52 (4.1)	0	0.02
Allocation			<0.001
Local	261 (21)	52 (41)	
Regional	617 (49)	68 (54)	
Extra-regional	386 (31)	6 (5)	
Rescue allocation	157 (12)	33 (26)	<0.001
Perfusion fluid			
UW	614 (49)	58 (46)	
HTK	559 (44)	58 (46)	
Other	91 (7.2)	10 (8)	0.85
	Mean (SD)	Mean (SD)	
Donor age (years)	46.8 (15.9)	41.2 (14.1)	<0.001
Height	173 (9.5)	175 (9.5)	0.049
BMI	24.6 (3.6)	24.3 (3.6)	0.47
GGT (U/L)	53 (82)	50 (69)	0.67
1st warm ischemia time (min)	n/a	13.2 (7.3)	
Cold ischemia time (hours)	8.9 (2.8)	7.2 (2.1)	<0.001
DRI	1.58 (0.39)	2.00 (0.38)	<0.001
without factor DCD*	n/a	1.33 (0.25)	
ET-DRI	1.65 (0.40)	2.13 (0.43)	<0.001
without factor DCD*	n/a	1.44 (0.29)	
	DBD	DCD	
Factor	N (%)	N (%)	p-value
Recipient sex			0.02
Male	810 (64)	94 (75)	
Female	454 (36)	32 (25)	
High urgent	184 (15)	6 (4.8)	0.002
Repeated transplant	192 (15)	6 (4.8)	0.001
	Mean (SD)	Mean (SD)	
Recipient age (years)	51.6 (11.8)	53.0 (11.5)	0.42
MELD	19.5 (9.9)	16.2 (7.8)	0.004

*not applicable since this only applies for DCD donors; value is equal to value above (DRI 1.58, ET-DRI 1.65)

Table 2: Death un-censored graft survival and patient survival after DBD and DCD liver transplantation

	N (%)	Graft survival (95% Confidence Interval; p=0.038)		
		1 year	5 years	10 years
DBD	1168 (90)	77.7 (75.3 – 80.1)	65.6 (62.8 – 68.4)	47.3 (43.1 – 51.5)
DCD	124 (10)	74.8 (67.0 – 82.6)	54.4 (45.4 – 63.4)	44.2 (34.6 – 53.8)

	N (%)	Patient Survival (95% Confidence Interval; p=0.59)		
		1 year	5 years	10 years
DBD	1174 (90)	82.8 (80.6 – 85.0)	71.4 (68.6 – 74.2)	52.6 (48.4 – 56.8)
DCD	124 (10)	87.8 (81.8 – 93.8)	68.1 (59.5 – 76.7)	55.9 (45.9 – 65.9)

Table 3 causes of death or retransplantation for DBD and DCD liver transplants

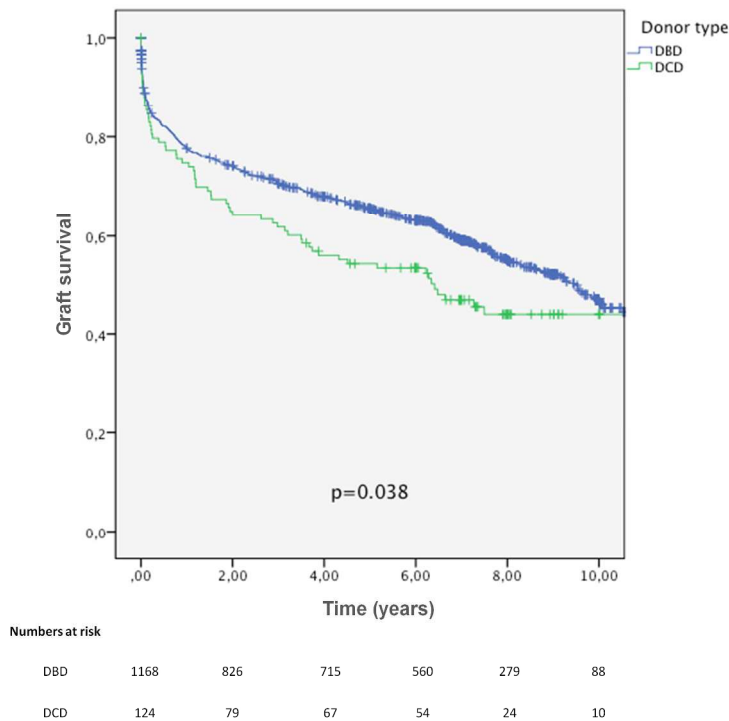
	DBD	DCD	
	N=1264	N=126	p-value*
Causes of graft loss	N (%)	N (%)	
Death	424 (34)	48 (38)	0.83
MOF/ARDS/sepsis	79 (6.3)	8 (6.3)	
Infection	48 (3.8)	8 (6.3)	
Cardiac	31 (2.5)	3 (2.4)	
Malignant	98 (7.8)	13 (10)	
Other	115 (9.1)	10 (7.9)	
Unknown	53 (4.2)	6 (4.8)	
Retransplantation	73 (5.8)	18 (14)	0.002
Thrombosis	22 (1.7)	1 (0.8)	
PNF	9 (0.7)	4 (3.2)	
NAS	7 (0.6)	8 (6.3)	
Rejection	5 (0.4)	-	
Other	8 (0.6)	3 (2.4)	
Unknown	22 (1.7)	2 (1.6)	

*p-value of chi-square analysis of sub-groups in cause of death or cause of retransplantation

Table 4: Kaplan-Meier survival analysis of warm ischemia time categories (N=123, p=0.12)

Warm ischemia time	N (%)	5-years graft survival	HR (95% CI)
<10 minutes	34 (28)	56%	Ref.
10-15 minutes	40 (33)	58%	0.83 (0.44-1.55)
16-20 minutes	28 (23)	61%	0.86 (0.43-1.72)
21-25 minutes	15 (12)	43%	1.18 (0.52-2.70)
>25 minutes	6 (5)	17%	2.87 (1.06-7.73)

* 3 missing values out of 126 DCD transplants

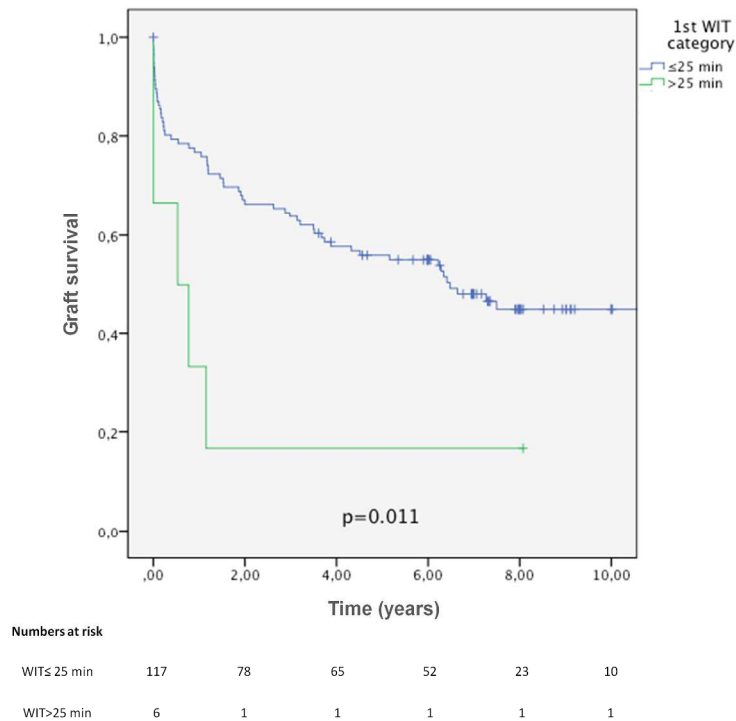


Long-term graft survival for DCD and DBD transplantations (log rank test $p=0.038$)

- Green line: DCD transplantations
- Blue line: DBD transplantations

254x190mm (300 x 300 DPI)

Accepted



Long-term graft survival for first warm ischemia time categories (log rank test $p=0.011$)

- Green line: 1st WIT >25 minutes
- Blue line: 1st WIT ≤25 minutes

254x190mm (300 x 300 DPI)